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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,564	11/01/2005	Trent Martin Woodruff	38871.33	1407

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EXAMINER	
KHANNA, HEMANT	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,564	WOODRUFF ET AL.	
	Examiner	Art Unit	
	Hemant Khanna	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event; however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-16 and 19-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 11-16, 19-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Applicant's remarks filed March 30, 2007. Applicant has cancelled claims 17-18 to overcome Examiner's rejection under 35 USC 112, second paragraph. Further, the applicant has amended claim 1 to overcome Examiner's rejection under 35 USC 112, first paragraph.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

3. Claims 1-9, 11-16, 19-24 have been examined on the merits.

Claim Objections

4. (New) Claim 13 is objected to because of the following informalities: the notation of numbers to represent compounds is unclear. For the benefit of clarity, Applicant is asked to refer to the notations with compound names or chemical formula's. Appropriate correction is required.

Claim 14 is objected to because of the following informalities: the notation of "described in PCT/AU02/01427" to denote the prior disclosure of compounds is improper. For the benefit of clarity, Applicant is asked to refer to the compound numbers with names or chemical formula's. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. (Withdrawn) Rejection of claim 17-18, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which the Applicant regards as the invention is withdrawn in view of Applicant's cancellation of claims 17-18.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. (New) Claims 1-9, 11-16, 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for antagonists of C5a receptor for the claimed treatment of inflammatory bowel disease, does not reasonably provide enablement for any antagonist represented by formula 1 having agonist activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with claim 1.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed

invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Nature of the invention. In the instant case, the claims are drawn to method of treating inflammatory bowel disease comprising the administration of antagonists of C5a receptor represented by compounds of formula 1, having substantially no agonist activity.

Breadth of the claims. According to the language of the claims, the scope of the method of treatment is very broad and can be extrapolated to any and all compounds of formula I, encompassing those that have agonist activity.

State and un/predictability of the prior art. The claimed subject matter is lacking in predictability. The art (WO 99/00406, page 10, lines 1-5) describes compounds encompassed within the instant formula I represented by Nme-F-K-P-dCha-L-r (r is the side chain of d-arginine and would meet the limitation of bioisostere in instant claim 1), as agonists of C5a receptor for the treatment of cancers, viral or parasitic infections

(page 8, lines 10-15). The teachings of the prior art are being interpreted to mean that not all compounds encompassed within the broad scope of claim 1 are enabled for treatment of inflammatory bowel disease.

The specification (page 6, lines 1-5) discloses very broadly that bioisosteres are side chains in which the terminal guanidine or urea group is retained, but the carbon backbone is replaced by a group which has a different structure but is such that the side chain as a whole reacts with the target protein in the same way as the parent group.

In view of the above teachings a person of skill in the art would have no evidence that treatment of inflammatory bowel disease by agonists within the scope of the instant claims has any basis. It is presumed that the Applicant's intent is to treat inflammatory bowel disease with antagonists of C5a receptor, having no agonist activity.

Working examples. Although examples are disclosed in the specification that demonstrate the treatment of inflammatory bowel disease by the administration of AcF-[OpdChaWR], there is no evidence for the intended treatment of any and all diseases covered by structurally related agonists of C5a receptor encompassed within the scope of the claims.

Guidance in the specification. The specification provides little guidance regarding practice of the claimed treatment to extrapolate to any antagonist having agonist activity. There is a lack of predictability in the art regarding the use any and all antagonists of C5a receptor as encompassed by the broad scope of claim 1.

Amount of experimentation necessary. Given the unpredictability of the art in view of the use of agonists of C5a represented by formula I, and the lack of guidance

provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate with the scope of the claim. Although the applicants have identified an interesting method of treatment of inflammatory bowel disease, but essentially all of the work required to extrapolate the treatment to any and all C5a antagonists represented by the formula I has been left for others.

Relative Skill of those skilled in the art. In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a Ph.D. with several years of experience in the art. As the cited art would point to, even with a level of skill in the art that is Ph.D. predictability of the results is not invariable.

In consideration of each of the factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

8. Claims 1-9, 11-16, 19-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for methods to treat ulcerative colitis, does not reasonably provide enablement for the treatment for any and all diseases encompassed by "inflammatory bowel disease". The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Nature of the invention. The instant invention is to the treatment of inflammatory bowel disease by administering an effective amount of a compound of formula I.

Breadth of the claims. According to the language of the claims, the use of compounds of formula I would prevent any and all inflammatory bowel diseases at any time.

State and un/predictability of the prior art. The claimed subject matter is lacking in predictability wherein it would at best have invariable results regarding the prevention of inflammatory bowel disease. Applicant's specification defines treatment or treating to encompass prevention (page 10, lines 20-25). At the time the invention was made, the successful prevention of Crohn's disease, was not routinely obtainable by those skilled in the art. It is presumed that the Applicant's intent is to treat Crohn's disease and not prevent Crohn's disease by the administration of compounds of formula I. Since the success of the former reads on effectively predicting a condition that will result before the development of disease, the prevention is not enabled in view of the contemporary knowledge in the art. This is reflected by the findings in a published manuscript. Van Assche et al teach that as of 2007, "Inflammatory bowel diseases are chronically relapsing intestinal inflammatory conditions with a typical onset in young adulthood and with an unpredictable disease course that may lead to debilitating complications" (paragraph 1, page 49). Further, Van Assche teach that the "course of Crohn's disease is notably unpredictable at diagnosis" (left column, page 50). Moreover, Van Assche teach "The ideal compound to treat crohn's disease should be curative for affected patients or preventive for offspring at risk. Avaliable therapies and agents in development only tackle the inflammatory reaction and disease recurrence is inevitable. The likelihood that a curative therapy will be developed in the next 10 years is extremely low. If this goal cannot be achieved, the best available therapy will be highly efficacious at inducing and maintaining remission and at preventing complication (disease modifying)" (Current Research Goals, page 51). Since the only current relief from

Crohn's disease involves treating the inflammatory response with corticosteroids or an anti-TNF antibody (Current treatment and unmet medical need, left column, page 51), one skilled in the art would conclude that the aspect of "treating" any inflammatory disease cannot be expected in view of the knowledge in the art that suggests that if at present the curative goals cannot be achieved, then in future preventing complications from the disease will be the next best available therapy.

Working examples. The instant specification (pages 15-16 and page 23) describes the pre- and post administration of AcF-[OpdChaWR] to rats having induced colitis or post-administration of AcF-[OpdChaWR] to patients already having Crohn's disease. Hence the instant limitation is being interpreted as a method of "minimizing" Crohn's disease and "preventing" ulcerative colitis. "Minimizing" Crohn's disease by the said administrations is evidenced by the decrease *in vivo* Crohn's Disease Activity Index as described in the instant specification (page 23, lines 15-20).

Guidance in the specification. The specification provides little guidance regarding practice of the claimed methods to extrapolate means of prevention. There is a lack of predictability in the art regarding the prevention of Crohn's disease. The specification does not explicitly disclose a preventative endpoint in subjects undergoing treatment for Crohn's disease with the administration of compounds of formula I.

Amount of experimentation necessary. Given the unpredictability of the art in view of prevention of Crohn's disease by the administration of compounds represented by formula I, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention

commensurate with the scope of the claims. Although the applicants have identified an interesting use of the compounds of formula I with a role in treating ulcerative colitis, but essentially all of the work required to ultimately develop a prevention method has been left for others.

Relative Skill of those skilled in the art. In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a Ph.D. or M.D. with several years of experience in the art. As the cited art would point to, even with a level of skill in the art that is Ph.D. or M.D. predictability of the results is not invariable.

In consideration of each of the factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Objections

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hemant Khanna Ph.D.
June 15, 2007

DAVID LUKTON, PH.D.
PRIMARY EXAMINER